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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/539,728	04/05/2006	Tatu Utpal	8920-000025/US/NP	8602

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EXAMINER	
GRUN, JAMES LESLIE	
ART UNIT	PAPER NUMBER
1641	
MAIL DATE	DELIVERY MODE
02/20/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/539,728	UTPAL ET AL.	
	Examiner	Art Unit	
	JAMES L. GRUN	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 November 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

The amendment filed 12 November 2008 is acknowledged and has been entered. Claims 7-16 are newly added. Claims 1-6 have been cancelled. Claims 7-16 remain in the case.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention, and failing to adequately teach how to make and/or use the invention, i.e. failing to provide an enabling disclosure.

Claims 7-16 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

With regard to the invention as is now claimed, the specification, as originally filed, does not provide support for testing of "said protein bound test compound" as is now claimed. Applicant teaches unconnected determinations in which a matrix-immobilized test compound is tested for binding with the *Plasmodium falciparum* heat shock protein of approximately 90kDa (PfHSP90) and the test compound, free of the matrix and free of the PfHSP90 in parasite lysate, is tested for its ability to inhibit the growth of a *Plasmodium falciparum* culture. Absent any description or guidance in the specification as filed, one would not have explicit or implicit indication that testing of the test compound, immobilized and bound to PfHSP90, for parasite

growth inhibition was originally contemplated as part of applicant's invention and such does not satisfy the written description requirements of 35 U.S.C. § 112, first paragraph. Applicant is requested to direct the Examiner's attention to specific passages where support for these newly recited limitations can be found in the specification as filed or is required to delete the new matter.

Claims 7-16 are rejected under 35 U.S.C. § 112, first paragraph, for reasons similar to those of record set forth with regard to the similar subject matter of claims 1-6, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, particularly the invention commensurate in scope to that as is now claimed.

Applicant's specification provides no adequate teaching as to how one uses the method as disclosed and claimed for other than an ansamycin antibiotic that competes with ATP for binding to Plasmodial HSP90. Other than ansamycin antibiotics, one would have no ability to predict that compound binding to Plasmodial HSP90 has any significance in the functioning of the heat shock protein. The therapeutic potential based upon the mere detection of binding is entirely unknown because, other than inhibition of ATP binding, there would appear no art accepted mode of action that would allow one to predict from the in vitro binding assay portion of the method that binding to the PfHSP90 would have any effect on parasite growth in that portion of the method, or in vivo. Mere binding to a protein does not equate to binding in a manner that modulates whatever in situ or in vivo pathway that the protein affects. Many potential binding sites would be expected on a protein and thus mere binding would not correlate predictably to

any effect on parasite growth or any in vivo result. Identification of compounds which bind, or which promote or inhibit the binding of a ligand or associated protein, which produces no biological effect resultant from the binding interaction would not serve to identify any useful therapeutic. Conversely, many compounds which do not bind to PfHSP90 may have anti-malarial drug effects and be excluded by applicant's screening method. Applicant's specification provides a mere suggestion to one in the art to perform further random unpredictable experimentation to determine what PfHSP90 binding compounds, if any other than ansamycin antibiotics, affect parasite growth and are potentially functional as an anti-malarial drug. Such an invitation to experiment does not provide an indication that applicant had possession of the invention of the scope as claimed at the time the application was filed and does not provide an enabling disclosure for one to predictably screen other than ansamycin antibiotics with any assurance of success. The examiner would again note that even geldanamycin was ineffective against an in vivo *Plasmodium berghei* infection (DeBoer et al., J. Antibiotics 23: 442, 1970) and that applicant's assays with geldanamycin appear to involve the addition of dimethylsulfoxide.

Applicant's arguments filed 12 November 2008 have been fully considered but they are not deemed to be persuasive. Notwithstanding applicant's assertions to the contrary, applicant's disclosure that competition of ansamycin antibiotics with ATP for PfHSP90 binding inhibits parasite growth does not support an invention of the scope as is now claimed because there is nothing to connect the two different parts of the method and nothing to correlate mere binding to any predictable growth inhibition, it is binding at the site of ATP binding and competition therewith which suggests an anti-malarial activity for a PfHSP90 binding compound. Applicant

urges that predictability of in vivo activity is irrelevant for the screening method. This is not found persuasive because a compound which functions only in vitro in the presence of a permeabilizing agent such as dimethylsulfoxide has limited or no use as a "drug."

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 7-16 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 7 and claims dependent thereupon, "the presence" lacks antecedent basis. The interrelationships of the components and steps of the method are unclear because it is not clear what is encompassed by "said protein bound test compound" because said test compound that is bound is covalently immobilized to a matrix. In these claims it is believed that "saponin-freed" was intended.

In claim 11 and claims dependent thereupon, improper Markush language is used to claim the members of the group. The alternatives "or" or "selected from the group consisting of...and" are acceptable.

In claim 13 and claims dependent thereupon, "the number" of ring forms lacks antecedent basis.

In clams 14-16, recitations of "using" are not valid method steps.

In claims 15 and 16, the interrelationships of the components and steps of the method are not clear, e.g.: it is not clear how compound not immobilized is blocked; it is not clear to what

volume the TRIS buffer is equal; or, it is not clear how one detects a particular bound protein from a lysate to a compound of unknown binding. In claim 16, "said test compound of unknown structure" lacks antecedent basis.

Applicant's arguments filed 12 November 2008 have been fully considered but they are not deemed to be persuasive. Notwithstanding applicant's assertions to the contrary, applicant's amendments have not obviated rejections under this statute for the reasons set forth above.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
> (c) Subject matter developed by another person, which qualifies as prior art only under one or more subsections (e), (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.
>
> This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

Claims 7-13 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Jendoubi et al. (J. Immunol. 134: 1941, 1985) in view of Bonnefoy et al. (Mol. Biochem. Parasitol. 67: 157, 1994) and Banumathy et al. (J. Biol. Chem. 277: 3902, 2002) for reasons similar to those of record in the prior rejection of the similar subject matter of claims 1-4 and 6. In addition to the teachings of the references noted in the prior Office action: Bonnefoy et al. teach that the XIV-7 anti-PfHSP90 monoclonal antibody of Jendoubi et al. was functional for antigen binding when

used coupled to a Sepharose column for affinity purification of PfHSP90 (see e.g. page 166); and, Jendoubi et al. teach that the XIV-7 anti-PfHSP90 monoclonal antibody, in view of Bonnefoy et al., was tested with ring-stage synchronized *Plasmodium falciparum* parasite cultures to determine *in vitro* growth inhibition of the antibody compared to control cultures without the antibody (see e.g. pages 1942 and 1944). It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to have used saponin to free the parasites in the assays of Jendoubi et al., as modified by Bonnefoy et al., in view of Banumathy et al. for the reasons of record.

Applicant's arguments filed 12 November 2008 have been fully considered but they are not deemed to be persuasive.

Notwithstanding applicant's assertions to the contrary, the references clearly teach that an immobilized test compound which bound the *Plasmodium falciparum* heat shock protein of approximately 90kDa (PfHSP90) was also tested for its ability to inhibit the growth of the parasite. The combined teachings of the references clearly teach the method steps as positively recited in the instant claims.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (e.g., binding to the geldanamycin/ATP binding site of PfHSP90) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Moreover, with regard to limitations in dependent claims asserted by applicant as not shown in

the references, it is noted that limitations recited in the alternative are not required in the rejected method claims.

Notwithstanding applicant's assertions to the contrary, a clause merely reciting a desired result of a positively recited process step is not given weight and, as would have been obvious to one of ordinary skill in the art, not every compound binding to a given protein tested for inhibition of growth would be shown to inhibit parasite growth.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR REPLY TO THIS FINAL ACTION IS SET TO EXPIRE **THREE MONTHS** FROM THE MAILING DATE OF THIS ACTION. IN THE EVENT A FIRST REPLY IS FILED WITHIN **TWO MONTHS** OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE **THREE-MONTH** SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR REPLY EXPIRE LATER THAN **SIX MONTHS** FROM THE MAILING DATE OF THIS FINAL ACTION.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James L. Grun, Ph.D., whose telephone number is (571) 272-0821. The examiner can normally be reached on weekdays from 11 a.m. to 7 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya, SPE, can be contacted at (571) 272-0806.

The phone number for official facsimile transmitted communications to TC 1600, Group 1640, is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application, or requests to supply missing elements from Office communications, should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/J. L. G./
James L. Grun, Ph.D.
Examiner, Art Unit 1641
February 20, 2009

/Ann Y. Lam/
Primary Examiner, Art Unit 1641
February 14, 2009